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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/533,017 | 12/12/2005 | Maria Cristina Geroni | 18086 | 9303 |

23389 7590 02/19/2009

SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

| EXAMINER | |
|---|---|
| FINN, MEGHAN R | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 02/19/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/533,017 | GERONI ET AL. | |
| | Examiner | Art Unit | |
| | MEGHAN FINN | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,5,7 and 11-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5, 7, 11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Applicant's Amendment filed November 25, 2008 has been received and entered into present application. No claims were canceled or added, thus claims 1, 3, 5, 7, and 11-14 are still pending.

Applicants' arguments, filed November 25, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the previous rejection mailed August 25, 2008, claim 1 was rejected for containing new matter because "to those patients whose CYP3A levels indicate formation of a metabolite of nemorubicin more active than nemorubicin" is not supported

in the originally filed disclosure. Applicants have argued that the experimental section (pages 2-4) teaches that only CYP3A4 metabolizes nemorubicin and that the metabolism of nemorubicin correlates with CYP3A4 levels (page 3). They further argue that since CYP3A levels correlate with the metabolites of nemorubicin that "by common sense" this includes the more active metabolite of nemorubicin. This argument is confusing because nowhere has applicant indicated that there was ever disclosure of the fact that CYP3A levels indicate formation of a metabolite that is more active than nemorubicin. CYP3A levels indicate that nemorubicin is being metabolized, and in other parts of the specification applicant indicates that some metabolites of nemorubicin are more potent than nemorubicin but nowhere is the idea that the CYP3A level indicates formation of a more active metabolite ever presented and is thus new matter. Applicant's arguments were carefully considered but not found to be persuasive and thus the rejection of claim 1 is **maintained.**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, 7, and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (Cytochrome P-450…) in view of Beulz-Riché et al. (Effects of paclitaxel…), in further view of Pacciarini et al. (WO 00/15203), each already of record in pages 3-5 of the previous action mailed August 25, 2008, of which reasons are herein incorporated by reference.

In the previous rejection, claims 1, 3, 5, 7, and 11-14 were rejected over Collins et al. in view of Beulz-Riche et al. in further view of Pacciarini et al. The claims remain the same and the rejection still applies as detailed in the office action of August 25, 2008. Applicant has argued that Collins et al. is inappropriate because it teaches a method that measures CYP3A levels to screen patients who are too sensitive to docetaxel whereas applicant's invention is using CYP3A levels to optimize therapy with nemorubicin. This argument is not found persuasive because Collins et al. is relied upon for teaching that drugs which are metabolized by CYP3A (such as docetaxel and nemorubicin) can be evaluated by CYP3A levels to determine how fast a patient is

metabolizing that drug. The fact that Collins et al. is using this to determine patients who metabolize something too fast versus the appropriate rate is not an issue because the teaching that one of ordinary skill in the art at the time of the invention would take away from Collins et al. is that CYP3A levels can be used to measure the metabolism of the drug. One of ordinary skill in the art at the time of the invention would have recognized that the method of Collins et al. could be used for other drugs that are known to be metabolized by CYP3A and that it could be used to identify slow, proper, and too rapid metabolization of a drug.

Applicant has made the argument that the effectiveness of a method of individualizing doses of an anticancer drug according to the levels of the metabolizing enzyme, depends on the type of anticancer drug, the nature of the metabolite of the same drug, and the intended mechanism of the treatment and that if one of these factors is different from one art to the other that one of skill in the art would be "unable to utilize the same method as in the prior art to effect the intended method'. The last statement of this argument is confusing and it is not clear what applicant is attempting to argue. It appears that applicant is saying that since all three of the above conditions mentioned are not the same in Collins et al. and the instant invention that it does not make the invention obvious. However, this argument is not found persuasive because the method of Collins et al. is not relied upon to teach the entire claimed method, only the step of determining the amount of rate of a drug metabolized by CYP3A by measuring said levels. This could easily and clearly be used for another drug, and the motivation to use such a method to individualize a drug treatment is well known in the

art, and was discussed in the previous office action. The fact that the metabolite of Collins et al. is inactive and that the metabolite of nemorubicin is more active is not something which would lead one of ordinary skill in the art to discount the method of Collins et al. as it is the amount of the drug being metabolized that is key to the measurement not the effect afterwards. The key idea taught by Collins et al. is that that one can measure the CYP3A levels and determine how much/fast a drug is being metabolized by the particular patient since metabolization varies greatly from patient to patient.

Applicant's arguments were carefully considered but not deemed persuasive and thus the rejection of claims 1, 3, 5, 7, and 11-14 is **maintained.**

***Conclusion***

Rejection of claims 1, 3, 5, 7, and 11-14 is deemed proper and is **maintained.**

No Claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 9:30am-7pm Mon-Thu, 9:30am-6pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614